The 100,000 Genome Project

Dr Dorothy Goddard
Dr Mark Beresford
The 100,000 Genomes Project was officially launched in 2013.

The project aims to sequence 100,000 genomes of about 75,000 people by the end of 2017.

Focus on rare disease (patients and their families) and cancer.

**Aims:**
To create and new genomic medicine service for the NHS

And enable new medical research…
- Combines genomic sequencing with medical records – largest in the world
- Study how best to use genomics in healthcare
- Investigate causes, diagnosis and treatment of disease
- Develop a UK genomics industry – transformation of the way we manage disease
What is genomics?

- Genetics is the study of the way particular features or diseases are inherited through genes passed down from one generation to the next.

  Groups of genes work together - their activity influenced by environmental and other factors.

  The DNA links between genes also very important.

  Almost every healthy cell in your body has a complete set of genes.

  One set of all these genes (plus the DNA between the genes) is called a genome.
What is genomics?

- **Genomics** is the study of the whole genome and how it works.
- Includes how the genome is interpreted and the technologies that have been developed to help with this.
- Human genome sequenced and published for first time in 2003, taking 13 years to achieve at a cost of over £2bn. Advances in technology mean the human genome can now be sequenced within 15 minutes for less than £1000.
- Human Genome Project demonstrated only about 20,000 genes – remaining (significant amount) DNA important role, influencing, regulating and controlling the rest.
- Important therefore, to sequence the whole human genome (rather than just looking at the 20,000 genes currently used for diagnosis in medicine) to really understand the role of genes in health and disease.
100,000 Genomes Project

- By sequencing the genome of an individual:
  - Possible to **predict how well a person will respond** to a treatment
  - Find the **most effective treatment**, allowing targeted therapy
    - more cost effective
    - improved outcomes.

- Genomic medicine will support further research and development into new and better treatments and drugs.
What can the NHS provide?

- People are very different, so studying a small number of genomes would not be enough to give a true picture of our genes and their relationship to disease.

- Also important to know more about the person whose genome is studied:
  - disease symptoms and when they first started
  - physiological measurements, such as heart rate or blood pressure
  - past medical history/previous illnesses
  - medications
  - birth weight

- NHS can link medical records with a person’s genome data – on a large scale.
100,000 Genomes Project

- To bring predicted benefits of genomics to NHS patients: Prime Minister announced the Project in late 2012

- Genomics England (company wholly owned and funded by the Department of Health) set up to deliver this flagship project:
  - to sequence 100,000 whole genomes from NHS patients by 2017

- Genomics England aims:
  - to create an ethical and transparent programme based on consent
  - to bring benefit to patients and set up a genomic medicine service for the NHS
  - to enable new scientific discovery and medical insights
  - to kick start the development of a UK genomics industry
Genomic Medical Centres

- Genomic Medical Centres (GMCs) set up to identify, recruit, consent and take blood or tissue samples from people eligible for the project.
- 11 genomic medical centres (wave 1) + 2 more (wave 2)

- The West of England Genomics Partnership was established to bid for a Wave 2 designated GMC
  - West of England Academic Health Science Network
  - Universities of West of England, Bristol and Bath
  - Clinical Commissioning Groups for Bristol, North Somerset, South Gloucestershire, Gloucestershire and Bath and North East Somerset
  - NHS England South West,
  - Local Delivery Partners (LDPs): North Bristol Trust, UH Bristol, RUH and Gloucestershire
  - Patient Organisations,
WE Genomic Medicine Partnership

- Established in April 2015
- Serve the population of the West of England
  - Bath, Bristol, Gloucestershire and Weston Super Mare
- Population coverage for cancer is 2 million (and for ‘rare disease’ is 2.7 million)
- WEGMP will deliver the GMC in 2 phases, planning to start recruiting in Bristol from January 2016 with an expectation that RUH will come on line from September 2016
- Not yet finally approved………NHSE assessment visit 19th November!
Cancer pathway
## Cancer types and recruitment

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Potential recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>715</td>
</tr>
<tr>
<td>Colorectal</td>
<td>492</td>
</tr>
<tr>
<td>Lung</td>
<td>413</td>
</tr>
<tr>
<td>Ovarian</td>
<td>89</td>
</tr>
<tr>
<td>Prostate</td>
<td>589</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>0</td>
</tr>
<tr>
<td>Renal</td>
<td>92</td>
</tr>
<tr>
<td>Childhood</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>2408</td>
</tr>
</tbody>
</table>

### Assumptions
- Recruitment of 15% of eligible patients
- Roll out of complex pathway
- A biopsy sample is sufficient
- Sample failure rate of 40%

NB: there is no evidence from other GMC regarding any of the above assumption
Cancer types and likely pathway

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Simple</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Simple</td>
</tr>
<tr>
<td>Lung</td>
<td>Complex</td>
</tr>
<tr>
<td>Ovarian</td>
<td>Simple</td>
</tr>
<tr>
<td>Prostate</td>
<td>Complex</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>Simple</td>
</tr>
<tr>
<td>Renal</td>
<td>Simple</td>
</tr>
<tr>
<td>Childhood</td>
<td>Complex</td>
</tr>
</tbody>
</table>

Simple Pathway:
- Surgery is primary treatment modality

Complex pathway:
- Primary chemotherapy in metastatic disease
- Primary radiotherapy, e.g., prostate cancer
- Difficulty in obtaining a biopsy
Pathway - Cancer

Start

Cancer Referral

Send PIS with OPA letter

Outpatients Appointment

Biopsy taken

Results Clinic

Tumour appropriate?

No

Continue with hospital treatment

Chemotherapy

Radiotherapy

Follow Up

6) Results & Further Care

Non-surgical treatment

Take Genomic samples and store

Assess if suitable

Sample from intermediate storage

MDT - no pt. attendance

Participant identified and recruitment reviewed

Pt. Identifier

Hospital ID

Date

End

Date extracted

Transport

Timing

Processing data

Conclusions

4) Lab Processing, Blood DNA & Omics

5) Lab Processing, Tumour
Challenges

- Engagement of wide range of clinicians and clinical services
- Limited funding for additional resources
- Logistics of sample handling and transport
- Possible inadequacy of biopsy samples
- National tumour site GeCIPs not yet decided on exact requirements of patient types
Challenges

- Complicated consent process
- Potential finding of unexpected genetic defects/risks
- Data handling/security/commercial access
- Quality of high-throughput sequencing
- Quantity of data to store
West of England Academic Health Science Network
Universities of West of England, Bristol and Bath
Clinical Commissioning Groups for Bristol, North Somerset, South Gloucestershire, Gloucestershire and Bath and North East Somerset
NHS England South West,
Local Delivery Partners (LDPs): North Bristol Trust, UH Bristol, Weston, RUH and Gloucestershire
Patient Organisations,